Ph.D. SYNOPSIS (2024)

RESEARCH STUDENT	**Mr. SURAJ RAMCHANADRA SHINDE**
MAILID.	surajshinde115@gmail.com
MOBILENO.	9096073200
CATEGORY	OPEN
SUBJECT	PHARMACEUTICAL SCIENCES & TECHNOLOGY
Ph.D. SYNOPSIS TITLE	"FORMULATION, DEVELOPMENT AND EVALUATION OF NANOSTRUCTURED LIPID CARRIERS FOR TOPICAL APPLICATION"
RESEARCH GUIDE	**PROF. Dr. NAGOBA S. N.**
MAILID.	nagobashivraj@gmail.com
MOBILENO.	+91 9637908901
DESIGNATION	PROFESSOR AND HEAD,DEPT. OF PHARMACEUTICS, CHANNABASWESHWAR PHARMACY COLLEGE (DEGREE), KAVA ROAD, LATUR.
RESEARCH CENTRE	CHANNABASWESHWAR PHARMACY COLLEGE (DEGREE), KAVA ROAD, LATUR.
UNIVERSITY	SWAMIRAMANANDTEERTHMARATHWADAUNIVERSITY, NANDED-431606, (MAHARASHTRA STATE), INDIA.
DATEOF R.A.C.	23/08/2023
DATEOF R.R.C.	20/12/2024
PLACEOF R.R.C.	**S.R.T.M. UNIVERSITY, NANDED.**

"FORMULATION, DEVELOPMENT AND EVALUATION OF NANOSTRUCTURED LIPID CARRIERS FOR TOPICAL APPLICATION"

A SYNOPSIS SUBMITTED FOR THE REGISTRATION OF

DEGREE OF DOCTOR OF PHILOSOPHY

In The Faculty of Pharmaceutical Sciences & Technology

By

Mr. Suraj Ramchandra Shinde

M.Pharmacy (Pharmaceutics)

Under the Guidance of

Prof. Dr. Nagoba S.N.

M. Pharm. Ph.D.

Professor and Head Dept.of Pharmaceutics

Channabasweshwar Pharmacy College (Degree),

Kava Road, Latur.

Swami Ramanand Teerth Marathwada University,

Nanded-431606, (Maharashtra State), India.

2024

INDEX

SRNO	CONTENT	PAGENO
1	ABSTRACT OF PROPOSED WORK PLAN	4
2	INTRODUCTION	5-8
3	REVIEW OF LITERATURE	9-11
4	OBJECTIVES OF RESEARCH /PROPOSED HYPOTHESIS	12
5	PLAN OF WORK	13
6	MATERIALS AND METHODOLOGY	14
7	IMPORTANCE OF STUDY/SOCIETY APPLICATION/ SIGNIFICANCE OF THE STUDY	14-15
8	PROPOSED WORK PLAN/STRUCTURE OF STUDY	16
9	REFERENCES	17-18

ABSTRACT OF PRAPOSED WORK PLAN/ PROBLEM:

The aim of proposed research work is to formulate and evaluate nano-structured lipid carrier (NLC) containing potent drugs such as poorly soluble, antifungal, bacterial, psoriasis, dermatitis etc. which have severe side effects on healthy organizing body. There are many conventional dosage forms available in market such as tablet, capsule, etc. But these conventional treatments are coupled with so many toxicities and side effects related with drug for e.g. bulk drug requirement to have efficacy of treatment, drug wastage due to hepatic or in vivo degradation, deposition of drug in body show unwanted toxicity. So, there is a need to culminate hindrances of conventional dosage form by formulating a targeted drug delivery such as carrier approach like liposome, niosome, phytosome, erythrocytes, microspheres, pharmacosomes, solid lipid nanoparticle, nano-structured lipid carrier, etc. Amongst these, nano-structured lipid carrier can strongly immobilize drugs and prevent the particle from coalescing by virtue of the lipid matrix. Nano-structured lipid carrier show strong potential to target drug selectively without affectingnormal cell thereby minimizing drug toxicity.

Nano-structured lipid carrier are beneficial to increase bioavailability being biologically inert, non immunogenic in nature. Based on literature survey, we found that number of available drug have bioavailability issue with conventional form and to work on this, it is need to develop NLCs. Drug containing nano- structured lipid carrier will be prepared by homogenization technique or membrane contractor technique or double emulsification method or sonication etc. Nano-structured lipid carrier formulation will be evaluated and optimized on basis of various physicochemical parameter like particle size, SEM, TEM, DSC, FTIR, Zeta potential, entrapment efficiency, drug content, in-vitro and in vivo study and stability studies.

INTRODUCTION:

NLC possess numerous features that are advantageous for topical route of application these carriers are composed of physiological and biodegradable lipids exhibiting low systemic toxicity and low cytotoxicity. Most of the used lipids have an approved status or are excipients used in commercially available topical cosmetic or pharmaceutical preparations. The small size of the lipid particles ensures close contact to stratum corneum and can increase the amount of drug penetrating into skin. Due to their solid lipid matrix, a controlled release from these carriers is possible. This becomes an important tool when it is necessary to supply the drug over prolonged period of time, to reduce systemic absorption, and when drug produces irritation in high concentrations. As a result of film formation after topical application, occlusive.[2]

NLC matrix is composed of mixture of spatially different lipid molecules, normally mixture of solid and liquid lipid, which makes more imperfection in the matrix to accommodate more drug molecules than SLN. Despite the presence of liquid lipid, NLC matrix is solid at room/body temperature. It is expected that the drug-loading capacity will be enhanced, drug expulsion during storage will be minimized due to the imperfect crystal lattice and drug release profile can be easily modulated by varying the lipid matrix composition.[1]

The nano-delivery system is generally divided into two groups polymer based, lipid based. In case of polymer based nano-delivery it possesses some limitation such as the number of products based on former are very rare in the market due to the toxicity of polymer, sometimes lack of suitable large scale production. So, due to this reasons currently greater focus is to use the lipid-based nano-delivery systems like nano-emulsion, micro-emulsion, liposomes, SLN, NLC etc.[4] Among all of these NLC has greater approach to use in the cosmetic & topical preparation. Now a day's nano particles are incorporated in cosmetic and topical field because of their benefits such as increased efficiency, transparency, unique texture and protection of active ingredient so, leads to higher consumer compliance.[2]

For the past few decades, particulate systems like liposome, niosome, nanosphere, nanocapsule and nanoparticle have been used as a physical approach to alter and improve

the pharmacokinetic and pharmacodynamics properties of various types of drug molecules. Among all colloidal drug carriers nano-structured lipid carrier are gaining more popularity because of their stability, ease of preparation, for achieving reduced toxicity, for increased drug efficacy & site targeted action.

They have been used in vivo to protect the drug entity in the systemic circulation, restrict access of the drug to the chosen sites and to deliver the drug at a controlled and sustained rate to the site of action. Various lipids have been used in the formulation of nano-structured lipid carrier for drug delivery research to increase therapeutic benefit, while minimizing side effects.[5] The major goals in designing nano-structured lipid carrier as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen. Nano-structured lipid carrier is a very useful strategy towards targeted drug delivery, particularly in topical application like Antifungal, Bacterial, Psoriasis, Dermitises etc. In immunogenic diseases like HIV, AIDS, cancer and In metabolic disease such as diabetes mellitus treatment where in, the limiting factor is traditional lack of selectivity of drugs towards target site.

Nanostructured lipid carrier, particularly those coated with hydrophilic polymer such as poly(ethylene glycol) (PEG) known as long circulating particles, have been used as potential drug delivery because of their ability to circulate for a prolonged period time, target a particular organ, and can able to deliver DNA, peptides, enzymes and vitamins as well as hydrophobic API.[6] The unique nano-scale structure of nanostructured lipid carrier provides significant increases in surface area to volume ratio as well as its strong drug immobilizing property in lipid matrix notably improve, both in-vitro and in-vivo performance,as compared to the traditional drug delivery.

Basics of NLC:

Nanostructured lipid carriers (NLCs) are novel pharmaceutical formulations which are composed of physiological and biocompatible lipids, aqueous phase and surfactants. However, selection of the components and their ratios can particularly influence the final behavior of the developed formulation. Regarding lipid phase, it consists of an imperfect solid lipid matrix prepared by mixing solid and liquid lipids. There are various types of lipids that had been used in formulations of NLCs such as triglycerides, partial glycerides, fatty acids, steroids and waxes. Oils (liquid lipids) and fats contain mixtures of mono-, di- and triglycerides of fatty acids of different chain length and degree of unsaturation.

Components of NLC Drug Delivery System

Solid lipids	Stearic acid, Glyceryl monostearate, Cetyl palmitate, Glycerol behenate, Glycerol palmitostearate, etc
Liquid lipids	Oleic acid, Soy bean oil, Almond oil, Squalene, Caprylic/Capric triglycerides, Caraway essential oil, etc
Surfactants	Phospholipids: Soy lecithin, egg lecithin and phosphatidylcholine, etc Ethyleneoxide/propylene oxide copolymers: Poloxamer 188, poloxamer182, poloxamer 407 andpoloxamine 908, etc Sorbitan ethyleneoxide/propyleneoxide copolymers:Polysorbate20, polysorbate60 and Polysorbate 80, etc Alkylaryl polyether alcohol polymers: Tyloxapol, etc Bile salts: Sodium cholate, sodium glycolcholate, sodium tauro cholateand sodium tauro deoxycholate, etc Alcohols: Ethanol and butanol, etc

Advantages of NLC

1. Use of biodegradable and biocompatible lipids makes NLCs better to incorporate both Lipophilic and hydrophilic drugs.
2. Can control and target drug release at site.
3. NLCs can more strongly immobilize drugs and prevent the particle from coalescing by virtue of the lipid matrix compared to emulsions.
4. Since formulation does not contain high aqueous media NLCs show better physical stability.
5. Due to incorporation of drug into lipid matrix, In vivo as well as In vitro drug is protected till reaching site of action.
6. Higher drug loading capacity of NLCs makes it more appreciable.
7. As compared to other lipoidal nano particulates, drug expulsion during storage is very minute.
8. NLCs can be prepared without organic solvents.
9. Can be administered both via oral, topical and parentral route.

REVIEW OF LITERATURE

1) Xin Kong et.al (2015) had prepared **Betanethasone** dipropionate-loaded NLC was produced with precirol ATO 5 and oleicoil (OA) by melt emulsification method.. The *in-vitro* permeation study showed that 2.0% of Tween 80 increased the skin retention of BD. Meanwhile, when the proportion of Precirol ATO 5 and OA was 1:2, the BD-NLC showed highest skin retention. This study will facilitate the development of BDNLC, which may improve skin retention, reduce the adverse effects induced by systemic absorption and reduce skin irritation.[3]

2) Bharti Gaba et al. (2015) had prepared and evaluated Terbinafine HCl (TH)- loaded nanostructured lipid carrier (NLC) for the treatment of fungal infection via topical administration. TH-NLC was prepared using high pressure homogenization technique using Glyceryl Monostearate (GMS) as solid lipid, Labrasol as liquid lipid and Pluronic F-127 as surfactant. It was investigated that TH loaded NLCs were capable of reducing the fungal burden. Therefore, it can be concluded that TH-NLC demonstrated to be potential formulation approach for treating fungal infection in contrast to commercially available product.[4]

3) Siriporn Okonogi et al (2014) had prepared the lycopene-loaded NLC by hot temperature high pressure homogenization (HPH) technique. The entrapment efficiency was >99% for all tested 499 lycopene concentrations. It was found that NLC showed a biphasic 500 release pattern characterized for a fast release during the first 501 6 h followed by a slower release during the next 18 h. The 502 occlusion increased with increasing lycopene loading in the NLC 503 formulations.[5]

4) Atul Anand Phatak (2013) had prepared Nanostructured lipid carriers of Aceclofenac by hot sonication method technique followed by ultrasonication. They investigated that it was possible to prepare stable and effective lipid nanostructures with mixed lipids like Compritol 888 ATO and PEG-8 Miglyol 812. The DSC and FTIR analysis showed that the matrix cores of aceclofenac loaded NLC were less ordered arrangements of crystals and compatible respectively. The studies confirm the potential of the nanostructured lipid form of poorly water soluble drugs for the topical application. [6]

5) Shubham Uprit. et al (2013) had prepared, Nanostructured lipid carriers based gel of Minoxidil The nine different formulations of Minoxidil-NLC (NLC1–NLC9) were prepared using solid and liquid lipids with Cholesterol and Soya lecithin in different concentrations by the melt dispersion ultrasonication method. The NLC-based gel containing minoxidil dissolved in a mixture of solid lipid and liquid lipid in the nanoparticulate form helped us to attain the objective of faster onset yet prolonged action as evident from in vitro release.[7]

6) A.I. Mendes et al. (2013) had prepared miconazole-loaded nanostructured lipid carriers (NLC) dispersion was prepared and characterized. The dispersion was used to prepare a NLC-based hydrogel formulation proposed as an alternative system to improve the local delivery of miconazole to the oral mucosa. It was showed that the developed NLC dispersion presented particles in the nanometrics range, low PI values, good physical stability and with efficient ability for the encapsulation of miconazole. NLC in hydrogels demonstrated the achievement of desirable rheological features that benefit the therapeutic efficacy of the formulation, by increasing the retention time and easiness for topical application in the oral mucosa NLC allowed for the controlled miconazole release and the improvement of its antifungal activity, which results in a reduction of the dose required in each administration while minimize the undesirable side effects.[8]

7) S. Khurana et al. (2013) had developed a nanoemulsion (NE) gel formulation for the transdermal delivery of meloxicam (MLX) in order to ensure maximum controlled and sustained drug release capacity. It was showed that NE gel containing caprylic acid as oil

Phase is a suitable carrier system for the incorporation of meloxicam, and satisfies the best attributes for transdermal application and suitable release profile. The study suggests that caprylic acid based nanoemulsion gel could reduce the SC barrier effects and could enhance the transdermal permeation and penetration of MLX. MLX-NE gel exhibited excellent skin tolerance, hemocompatibility and significant efficacy in inflammation when compared to MLX solution.[9]

8) Yogeshwar G.et al (2009) had prepared microemulsion based gel for the vaginal delivery of fluconazole (FLZ). The solubility of FLZ in oils and surfactants was evaluated to identify components of the microemulsion. The FLZ-MBG could be successfully formulated for the topical treatment of vaginal candidiasis. The developed FLZ MBG did not show any vaginal irritation in rabbits proving its tolerability. The clinical studies indicated that FLZMBG could be a viable alternative to the current topical formulations available for the treatment of candidiasis.[10]

9) Medha Joshi et al. (2008) had designed Nanostructured lipid carriers (NLC) based topical gel of celecoxib was formulated for the treatment of inflammation and allied conditions.NLC prepared by the microemulsion template technique. It was showed that NLC gel exhibited faster onset yet effecting a prolonged action as evident from a comparative study with micellar gel with respect to *in vitro* release, *in vitro* permeation and pharmacodynamics studies.[11]

10) M. Joshi et al. (2006) had prepared Nanostructured Lipid Carrier (NLC)–based topical gel of Valdecoxib. NLCs prepared by microemulsion template technique were characterized by photon correlation spectroscopy for size. The sustained activity of the NLC-based gel even at the end of 24 h could be explained by the drug's encapsulation within the solid matrix, while the faster onset is explained by the drug's encapsulation in the oil and surfactant phase, which forms the outer phase of the dispersion.[12]

OBJECTIVES OF RESEARCH/ PROPOSED HYPOTHESIS:

Aim: "Formulation, Development, and Evaluation of Nanostructured lipid Carriers for Topical Application."

Objectives of the Research Work:

1. To perform preformulation study i.e. UV, solubility, FTIR, DSC, etc.
2. To formulate drug-loaded nanostructured lipid carrier drug delivery system.
3. To characterize drug loaded NLCs for % drug content, % drug entrapment efficiency, in vitro drug diffusion study, particle size, zeta potential, TEM, XRD, DSC etc.
4. To evaluate in-vitro study of optimized formulation in comparison with pure drug.
5. To carry out in-vivo a study of optimized formulation in comparison with pure drug.
6. To carry out histopathology study.
7. To conduct stability study.

PLAN OF WORK:

1. Literature review

2. Selection and Collection of drug & excipients

3. Pre-formulation Studies

a. Melting Point
b. Solubility study
c. UV Spectroscopy study
d. DSC
f. XRD
g. FTIR

4. Formulation development of NLCs

5. Evaluation of NLCs

- Appearance
- % Drug Content
- % Entrapment efficiency
- % In vitro drug diffusion
- Particle size
- Polydispersity index
- Zeta Potential
- XRD
- TEM
- In vitro study
- In vivo study
- Histopathology study
- Stability study.

MATERIALS AND METHODOLOGY:

1. Selection of drug:

e.g. Antifungal drug, Dermatological agent Antibacterial drug, topical antipsoriatics, Antiseptic and germicide, topical anesthetics, topical non-steroidal anti-inflammatory, topical emollient, topical anti-infective etc.

2. Polymer: Hyper cross linked Polystyerenes Cyclodextrines and its derivatives Copolymer like Poly (valerolactoneallylvalerolactone) and Poly (valerolactoneallyvalerolactoneoxepanedione) Ethyl cellulose, PVA

3. **Crosslinker**: Diphenyl carbonate, Dirylcarbonates, Diisocynates, Pyrromellitics anhydride, Carbonyldiimidazoles,Epichloridine,Glutaraldehyde, carboxylic acid, Diunhydrides, Dicloromethane.

Selection of a lipid:

To formulate the Nanostructured Lipid Carrier, following solid and liquid lipids will be selected e.g. Soybean oil or Oleic acid or Corn oil or Squaleneor Stearic acid etc.

Techniques used in preparation of Nanostructred lipid carriers gel:

There are several methods are used for preparation of nanostructured lipid carrier gel

1. High-Pressure Homogenization (HPH)
2. Solvent emulsification- evaporation method.
3. Phase Inversion method
4. High- speed homogenization and/or ultrasonication method.
5. Solvent Injection method.
6. Microemulsion method.
7. Coacervation method.

IMPORTANCE OF STUDY/SOCIETY APPLICATION:

- **International status:** Globally a nanostructured lipid carrier is an emerging area for novel applications in, topical and parenteral and oral drug delivery system. In combination with the evolution of its applications in large domains, nanoscience has been contributing itsremarkable role in drug delivery too. Recently, the global pharma world has witnessed marvelous development in introducing innovative nanotechnologies, exploring their applications in temporal and spatial drug delivery, addressing their toxicity concerns and resolving key federal issues. Nanostructured lipid carrier drug delivery systems, accordingly arc gaining widespread importance and popularity globally. There are potential applications of nanosystems in drug delivery areas like delivering in topical application.
- **US patent application 20170119891:** Nano-structured carriers for guided and targeted on-demand substance delivery (Granted on 04-05-2017).
- **South Korean patent application KR101777616B1:** Nano-structured Lipid Carrier comprising α-tocopherol (Granted on 13-09-2017).
- **National status:** The Global Burden of Disease project has shown that skin diseases continue to be the 4th leading cause of nonfatal disease burden world-wide. However, research efforts and funding do not match with the relative disability of skin diseases. International and national efforts, such as the WHO List of Essential Medicines, are critical towards reducing the socioeconomic burden of skin diseases and increasing access to care. Recent innovations such as teledermatology, point-of-care diagnostic tools, and task-shifting help to provide dermatological care to underserved regions in a cost-effective manner. Number of patients in India is increasing due to sedentary life style, poor living standard (diet & rest), pollution, lack of awareness early signs and symptoms etc. A big issue in India is lack of availability of most effective, safe and economic drug delivery for treatment of diseases either topical or systemic occurrence. Nanoparticulate, especially nano-structured lipid carrier have the potential to overcome the challenges related to conventional treatments. There is huge scope in India to develop a drug delivery with improved efficacy, biocompatibility, biodistribution and minimized toxicity in drug therapy.

SIGNIFICANCE OF THE STUDY:

Currently skin disease is one of the most common among all illnesses in humans and represents a huge public health problem on a global scale. There is a wide range of fungal infections, from superficial, affecting skin, skin appendages and mucous membranes, to systemic infections with invasion of internal organs. It is necessary to overcome these infections by selecting suitable drug delivery. The selection of vehicles is important for drug delivery to exert maximum activity and cause minimal adverse effects. Some novel Nano carriers are studied to load drugs for therapy. Among them, NLCs have gained much interest in recent years because of the satisfied drug carrier potency and safety. It is expected that the utility of NLCs in basic research and the clinical setting will be more extensive in the future because of urgent needs to discover new therapies such as treatments for fungal, cancer, neurodegenerative disease, and inflammation. Many investigations have examined lipid nanoparticle design for fewer side effects, longer half-life, and higher bioavailability compared to conventional carriers.

Table1The patents of NLCs for drug delivery application

Publication number	Title	Inventors	Publication date	Reference number
US20080020058	Lipid nanoparticles For the delivery of biologically active molecules	A1ChenT *etal.*	2008-01-24	**[13]**
US20100247619A1 WO2008000448A3	Nanostructured lipid carriers containing riluzole and pharmaceutical formulations containing said particles	Bondi' ML *etal.*	2010-09-30	**[14]**
US20110059157A1	Anionic lipids and lipid nano- structures and methods Of producing and using same	Awasthi Vand Lagisetty P	2011-03-10	**[15]**
WO2011116963A2	**Lipid nanoparticle capsules**	**Vila dot Petit V *etal.***	**2011-09-29**	**[16]**

PROPOSED WORK PLAN/ STRUCTURE OF STUDY

Sr. No.	Work	Period
1.	Literature survey	6 months
2.	Selection and collection of drug and Excipients	1 month
3.	Formulation of nanostructured lipid carriers	1 month
4.	Evaluation of nanostructured lipid carriers	3 months
5.	In vitro and in vivo study	6 months
6.	Statistical analysis, data interpretation and conclusions	6 months
7.	Publishing research and submitting data	6 months
8.	Data compilation, drafting of manuscript and thesis writing	7 months
	Total duration of work	36 months

REFERENCES

1. Jana Pardeike, Aiman Hommoss, RainerH. Müller Lipid nanoparticles(SLN,NLC) in cosmetic and pharmaceutical dermal products International Journal of Pharmaceutics 366 (2009) 170–184
2. Fardin Tamjidi , Mohammad Shahedi , Jaleh Varshosaz , Ali Nasirpour Nanostructured lipid carriers (NLC): A potential delivery system for bioactive food molecules Innovative Food Science and Emerging Technologies 19 (2013) 29–43
3. Xin Kong, Yuan Zhao, Peng Quan, Liang Development of a topical ointment of beta methasone dipropionate loaded Nanostructured lipid carrier Asian journal of pharmaceutical Sciences (2015)
4. Bharti Gaba, Mohammad Fazil, Saba Khan, Asgar Ali, Sanjula Baboota, Javed Ali Nanostructured lipid carrier system for topical delivery of Terbinafine Hydrochloride Bulletin of Faculty of Pharmacy, Cairo University (2015)
5. Siriporn Okonogi, Pornthida Riang janapatee Physicochemical characterization of lycopene-loaded nanostructured 3 lipid carrier formulations for topical administration International Journal of Pharmaceutics (2014)
6. Atul Anand Phata, Praveen Digambar Chaudhari Development and evaluation of Nanostructured Lipid Carrier (NLC) based topical delivery of an anti-inflammatory drug journal of pharmacy 7 (2015) 677-685
7. Shubham Uprit, Ram Kumar Sahu, Amit Roy, Aniruddha Pare Preparation and characterization of minoxidil loaded nanostructured lipid carrier gel for effective treatment of alopecia Saudi Pharmaceutical Journal (2013) 21, 379–385
8. A.I. Mendes, A.C. Silva , J.A.M. Catita , F. Cerqueira, C. Gabriel, C.M. Lopes Miconazole-loaded nanostructured lipid carriers (NLC) for local delivery to the oral mucosa: Improving antifungal activity Colloids and Surfaces B: Biointerfaces 111 (2013) 755– 763

9. S. Khurana, N.K. Jain, P.M.S.Bedi Nano emulsion based gel for transdermal delivery of meloxicam: Physico-chemical, mechanistic investigation Life Sciences 92 (2013) 383–392
10. Yogeshwar G. Bachhav, Vandana B. Patravale Microemulsion based vaginal gel of fluconazole: Formulation, in vitro and in vivo evaluation International Journal of Pharmaceutics 365 (2009) 175–179
11. Medha Joshi, Vandana Patravale Nanostructured lipid carrier (NLC) based gel of celecoxib International Journal of Pharmaceutics 346 (2008) 124–132
12. M.JoshiandV.Patravale Formulation and Evaluation of Nanostructured Lipid Carrier (NLC)–based Gel of Valdecoxib Drug Development and Industrial Pharmacy, 32:911–918, 2006
13. Xue HY, Wong HL. Tailoring nanostructured solid-lipid carriers for time-controlled intracellular siRNA kinetics to sustain RNA imediated chemo sensitization. Biomaterials 2011; 32: 2662-2672
14. Bondi' ML, Giammona G, Craparo EF, Drago F. Nanostructured lipid carriers containing riluzole and pharmaceutical formulations containing said particles. US20100247619, 2010
15. Awasthi V, Lagisetty P. Anionic lipids and lipid nano-structures and methods of producing and using same. US20110059157, 2011
16. Viladot Petit JL, Delgado González R, Fernández Botello A. Lipid nanoparticle capsules. WO2011116963, 2011
17. Khosa A, Reddi S, Saha RN. Nanostructured lipid carriers for site-specific drug delivery. Biomed Pharmacother. 2018;103:598–613.
18. Fu-Qiang Hu et al., Preparation and characterization of stearic acid nanostructured lipid carriers by solvent diffusion method in an aqueous system. Colloids and Surfaces B: Biointerfaces 45 (2005) 167–173.
19. X. Lin et al., Preparation and characterization of monocaprate nanostructured lipid carriers. Colloids and Surfaces A: Physicochem. Eng. Aspects 311 (2007) 106–111.
20. W.M. Obeidat et al., Preservation of nanostructured lipid carriers (NLC). European Journal of Pharmaceutics and Biopharmaceutics 76 (2010) 56–67.

Name of Research Candidate: Mr. Suraj Ramchandra Shinde	**Signature:**
Remarks of The Guide	satisfactory
Name and Designation of Research Supervisor: Prof. Dr. S. N. Nagoba Professor and Head, Department of Pharmaceutics, Channabasweshwar Pharmacy College (Degree), Latur.	**Dr. Nagoba S. N.** Research Guide, Professor & Head, Department of Pharmaceutics, Channabasweshwar Pharmacy College (Degree), Latur
Remarks of Director/ Principal Head of The School/Institution: Prof. Dr. Vijayendra Swamy S.M. Professor and Principal/Director, Department of Pharmaceutics, Channabasweshwar Pharmacy College (Degree), Latur.	**Dr. S.M. Vijayendra Swamy** Principal Channabasweshwar Pharmacy College (Degree), Latur